REMARKS/ARGUMENTS

Claims 53-63, 65-77 and 88 are pending in the application. Claims 53 and 66 have been amended. Claim 88 is new.

Examiner Interview

On December 10, 2010, the undersigned and patent attorney Barbara Gibbs, Ph.D. conducted a telephone interview with Examiner Laura Schuberg. As U.S. Patent No. 6,949,252 to Mizuno et al. ("Mizuno") was at issue, Dr. Gibbs began the interview by summarizing the disclosure of Mizuno. Dr. Gibbs explained that Mizuno teaches forming a solid matrix *in vitro*, adding cells to the matrix, and then culturing the matrix in a tissue processor. Once the tissue in the matrix has developed into neo-cartilage, it is then implanted. It was generally agreed during the interview that Applicants' inventive method does not require implanting a solid matrix of neo-cartilage. However, Examiner Schuberg noted that the claims were very broad and was concerned that they do not exclude the step of implanting a solid matrix of neo-cartilage.

In an attempt to arrive at claim language that would address the Examiner's concerns, it was agreed that reciting that the first polymerizable layer directly contacts the second polymerizable layer or similar language would overcome the rejection based upon Mizuno. Examiner Schuberg also suggested during the interview that specifying that the polymerizable layers are "injected" also appears to overcome Mizuno.

The undersigned and Dr. Gibbs would like to thank Examiner Schuberg for the helpful suggestions offered and the courtesies extended during the interview.

Claim Rejections, 35 U.S.C. § 103

Claims 53-63 and 65-77 have been rejected as obvious over Mizuno in view of U.S. Publication No. 20030077821 to Sah et al. ("Sah"), Anseth et al. (Journal of Controlled

Release 2002), U.S. Patent No. 5,916,585 to Cooke et al. ("Cooke") and U.S. Patent No. 6,773,723 to Spiro et al. ("Spiro").

Mizuno discloses methods for producing a multi-layered biological construct having an integration layer and a cellular support matrix layer. It may also optionally have a protection layer over the cellular support matrix layer. The integration layer is applied to the tissue and then the cell support is added to the integration layer, where it is adhered to the tissue through the integration layer. The cellular support matrix is a three-dimensional matrix in which cells are incubated to form a "neo-tissue" before being adhered to the tissue. Mizuno discloses that it is prepared by introducing the matrix into a solution of living cells such that the solution enters the sponge-like matrix by capillary action (column 2, line 65 to column 3, line 3; and column 3, lines 42 to 51). The Mizuno patent also states that "the cellular support matrix of the present invention acts like a sponge that wicks up (and evenly distributes throughout the intertices of the matrix) cells suspended in a sol-gel solution..." (column 11, lines 49 to 52). Moreover, the cell-infused matrix is then incubated to form a "neo-tissue" which is defined as a cellular composition that approximates the form and function of the tissue *in situ* (column 5, lines 54 to 56). Alternatively, cells may be grown into a three dimensional "neo-tissue" form without the use of the matrix before being used *in vivo.*

In contrast, the claimed method of the present invention provides a first polymerizable mixture having a first polymerizable material and first cells, where the mixture is directly placed in an osteochondral tissue space without being placed in a matrix or cultured before placement. It is then crosslinked to partially gel the mixture. The claimed method also provides a second polymerizable mixture having a second polymerizable material, the mixture directly placed with the partially gelled first layer and crosslinking it to partially gel the second mixture. It is contemplated that the first and second mixtures can be injected into the tissue space. See paragraph [0023]. In contrast, the cellular support matrix or neo-tissue of the Mizuno patent are solid and cannot be injected. Additionally, the matrix of Mizuno comprises cells and gel in a honeycomb structure, thus allowing only limited diffusion of any material from the optional layers on either side of the matrix into the matrix itself. Therefore, the integration layer and protection layer do not come in direct contact with each other.

Claim Amendments

In an effort to expedite prosecution of this application, but in no way conceding to the validity of the rejection, Applicants have amended independent claim 53 to recite *providing a second polymerizable mixture which comprises a second polymerizable material and directly placing a volume of the second polymerizable mixture in the tissue space in direct contact with the at least partially gelled first layer of hydrogel.* A similar amendment was made to claim 66.

Applicants have thus incorporated into claims 53 and 66 the language that was agreed upon during the interview. While the exact language "direct contact" is not used in the specification, support for the amendment is found, among other places, in ¶ [0137] of the application as published, which describes adding the second polymerizable layer B directly to partially gelled layer A as depicted in Fig. 7. The description and Fig. 7 fully support the amended claim language. Applicants thus respectfully request that the rejection be withdrawn.

As noted above, Examiner Schuberg suggested during the interview that specifying that the polymerizable layers are "injected" also appears to overcome Mizuno, noting that the solid three-dimensional matrix required by Mizuno must be implanted. Accordingly, Applicants have added new claim 88 to recite that the first and second polymerizable mixtures are placed by injection. Claim 88 is otherwise the same as claim 53 before this amendment. Support for this limitation can be found in Applicants' specification, e.g., at ¶ ¶ [0023], [0116] and [0117]. Mizuno, by contrast, teaches a second layer that is a solid tissue construct that must be implanted and cannot be placed by injection. Applicants thus respectfully request that new claim 88 be indicated as allowable.

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CONCLUSION

Claims 53 and 66 were amended per the agreement reached during the interview and new claim 88 is based upon Examiner Schuberg's helpful suggestion offered during the interview. Applicants thus submit that independent claims 53, 66 and 88 are all allowable and earnestly solicit allowance thereof. Since the dependent claims include all of the limitations of the allowable independent claims, Applicants request that the dependent claims also be allowed.

In the event the Examiner wishes to discuss any aspect of this response, she is invited to telephone the undersigned at the telephone number identified below.

☒ The Commissioner is hereby authorized to charge payment of the following fees with this communication or credit any overpayment to Deposit Account No. 02-3223:

☒ Any fees under 37 CFR 1.16 for the presentation of extra claims.

☒ Any fees for extension of time pursuant to 37 C.F.R. 1.17.

Respectfully submitted,

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